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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/981,313	10/15/2001	Kristina Marie Burow	36-001100US	4969

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EXAMINER	
SODERQUIST, ARLEN	
ART UNIT	**PAPER NUMBER**
1743	

DATE MAILED: 09/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/981,313	Applicant(s) BUROW ET AL.	
	Examiner Arlen Soderquist	Art Unit 1743	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 June 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-89* is/are pending in the application.

4a) Of the above claim(s) *75-89* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-74* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on *15 October 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *8-15-02,1-6-03*.

4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .

5) ☐ Notice of Informal Patent Application (PTO-152)

6) ☐ Other: _____.

1. Applicant's election without traverse of Group I in the reply filed on June 15, 2004 is acknowledged.

2. An issue of public use or on sale activity has been raised in this application. In order for the examiner to properly consider patentability of the claimed invention under 35 U.S.C. 102(b), additional information regarding this issue is required as follows: the published information that resulted in the copyright notification on page 1 of the instant specification. There is no indication of what has been published as copyrighted material or regarding the date of publication of the copyrighted material.

Applicant is reminded that failure to fully reply to this requirement for information will result in a holding of abandonment.

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 9-11, 13, 19-20, 22-23, 36-37, 42-43, 57-61 and 66-73 are rejected under 35 U.S.C. 102(b) as being anticipated by Sato (US 5,164,318). In the patent Sato teaches an automatic enzyme immunoassay analyzer in which a sample containing a non-labeled antibody (or a non-labeled antigen) is drawn into a probe having contained therein an antigen (or an antibody) to which a labeled antibody (or a labeled antigen) is bound. A competitive reaction takes place in the probe. The amount of the non-labeled antibody (or the non-labeled antigen) is measured from the enzyme activity of the labeled antibody (or labeled antigen) in a reaction solution that is discharged from the probe into a cuvette. Figure 1 shows the automatic analyzer of the invention which is designed to measure a very small amount of antigen in a serum sample, e.g. protein. As shown in the figure, this automatic analyzer has a probe stock rotary disk (1), a sample carrying rotary disk (2), a reactor rotary disk (3), a reagent carrying rotary disk (4), and a probe disposal box (5), which are disposed in an interrelated manner. Furthermore, the automatic analyzer is provided with a probe carrying arm means (6, first rotational robot) which moves in a controlled manner among the probe stock rotary disk, the sample carrying rotary disk, the reactor rotary disk, and the probe disposal box constituting a first work parameter. A drive

mechanism drives the arm means. A reagent carrying arm means (8, second rotational robot) reciprocating between the reactor rotary disk and the reagent carrying rotary disk has a pipette (81). This constitutes the second work perimeter. A hollow sampling probe (9, see figures 2-4), made of polypropylene is to be placed on the probe stock rotary disk 1. This sampling probe accommodates therein a multiplicity of micro-particles (95) made of a resin. An antibody complementary with the antigen to be measured is physically or chemically bound to the surfaces of the microparticles. Figure 5 illustrates in detail the probe carrying arm means. It has an arm (61), a carrying tube (62) provided at one end of the arm, and a swing axle (63) provided at the other end of the arm. The probe carrying arm means is swingable about the axis of the swing axle by means of a belt drive mechanism of a drive mechanism (7) (see figure 12) driven by a pulse motor, and is movable in the axial direction of the swing axle through a spline shaft drive of a pulse motor of the drive mechanism. The carrying tube has an outer diameter that closely fits with a serrated inner surface (91S) of the probe head (91), and then is capable of communicating with the inside of the probe body when engaged therewith. In addition, the carrying tube communicates with a piston-cylinder apparatus (64) through a passage (65) extending through the arm and the swing axle. The sample can be sucked into or discharged from the probe body by driving the piston-cylinder apparatus by means of a pulse motor (68) and a rack and pinion mechanism (66). The driving of the pulse motors for the probe carrying arm means and the piston-cylinder apparatus is controlled by a CPU (67). Figures 6-8 show the arrangement of the sample carrying rotary disk. A plurality of openings (21) are formed concentrically in the sample carrying rotary disc. Each of the openings is constituted by a smaller partial circular bore (211) having a diameter which is smaller than the outer diameter of the probe head and greater than the outer diameter of the probe body, a larger partial circular bore (212) disposed radially outwardly of the smaller bore and having a diameter which is smaller than the outer diameter of a large-diameter portion of a sample cup (22) which accommodates the sample and greater than the outer diameter of the probe head, and an arcuate slit (213) connecting the bores and having the same swinging curvature as that of the arm. Accordingly, the sampling probe and the sample cup can be placed on the disk at the respective bores. A cover disk (10) is disposed above the sample carrying rotary disk in such a manner as to provide a gap of about 1 mm between a top end of the probe head of the probe rested on the

disk and the lower surface of the cover disk. This cover disk has an outer diameter substantially equal to that of the sample carrying rotary disk and is stationary. Two openings (11) of substantially the same configuration as that of the opening (21) are formed radially in tandem at the portions of the cover disk opposing the opening of the sample carrying rotary disk. Figures 9A-9N and 9P describe the operation of the automatic analyzer. The reagent carrying arm means reciprocates between the reagent carrying rotary disk and the reactor disk so as to pipette a specific substrate (S) in the reagent carrying rotary disk into the cuvette (31) in the reactor disk. Consequently, the substrate is added to the free part in the cuvette to start the enzyme reaction. After a time, the cuvette is moved to a measurement position by the rotation of the reactor disk. The absorbance of the free part in the cuvette is measured by using a light source (32) and a spectrophotometer (33). It is possible to determine the amount of protein contained in the serum sample from the measured absorbance by referring to a calibration curve. Additional, formats include measuring an antibody by replacing the antigen on the resin particle with the antibody or coating the antigen or antibody on an inner surface of the probe body instead of the surfaces of the resin particles. Example are given showing the measurement of ferritin, insulin, cortisol, prostaglandin (PGF2α) and α-fetoprotein.

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* v. *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

5. Claims 1-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hutchins (US 5,928,952 or EP 915,341) in view of Ishibashi (US 5,087,423). Since the patent and

publication are part of the same patent family only the patent will be described however equivalent disclosure is found in the publication. In the patent Hutchins teaches a scheduled system and method for processing chemical products. The processing system is for processing a plurality of products, the system including a plurality of interchangeable units arranged to sequentially receive the products and each having a work station for effecting a specific operation on each of the products, the operation requiring a given time period; and wherein each work station accommodates simultaneously a predetermined number of the products, and the given time period and predetermined number associated with each unit are different than the given time periods and predetermined numbers of other said units. A transport system transports the products through the processing system so as to provide for each product a common occupancy time therein. In discussing prior robotic systems, column 1 lines 22-44 teach that the user of a robotic processing system first arranges processing stations in any convenient pattern and then instructs a robot in given processing actions. Even though programming tasks, once understood by an operator, are not intellectually challenging, the task of setting up a system to operate efficiently is laborious. As the number of stations in a system increased, the number of variables to keep in mind to avoid collisions and otherwise avoid conflicts in instruction made the task laborious even for those skilled in computer programming. In addition, many traditional robotic systems such as those used for drug screening operations utilize a single robotic device with a number of work stations, which perform operations requiring various time periods and may be repeated several times in a complete process. Consequently, the movement of product samples requires complex looping and scheduling for efficient operation which typically is attained by maximizing utilization time of the robotic device. Product throughput of such systems is limited, therefore, by available robotic device time. The object of the Hutchins device and method is to provide a robotic system significantly increasing product throughput of chemical processes such as drug screening. The device is substantially similar to the instant claims except that it does not teach non-sequential treatment of the samples.

In the patent Ishibashi teaches an automatic analyzing device having a plurality of analyzing modules, a plurality of analyzing routes and at least one bypass route bypassing at least one analyzing module. Each analyzing module is capable of analyzing samples with respect to one or more items, and samples successively supplied from the introduction sides of

the modules are selectively delivered into each module in accordance with the possible analyzing items of each module and the analyzing items of the samples to be analyzed. The sample cup can pass the module via a bypass or can be returned to the introduction side of the module via a bypass, in accordance with the items to be analyzed, the effective distribution of the sample cups can be performed. Column 1, lines 19-45 discuss known analyzing apparatus in which analyzing modules ranging from two to eight are serially arranged, and sample cups each containing sample liquids to be analyzed are successively conveyed to the modules one by one via only one route. Necessary amounts of the samples are picked up and delivered into reaction vessels in the modules according to the analyzing items of each sample that are to be analyzed by each module. Although it is not necessary to analyze all items for each sample, all samples have to be successively fed to each of the analyzing modules. Since the each module can analyze from four to twelve items, it is possible to analyze 20-30 items in the automatic analyzing apparatus as a whole. Generally, not all samples require the same analyzing items. In general, a sample requires only 50-60% of all possible analyzing items of the apparatus. In other words, 40-50% of the analysis capacity is not being used for each respective sample. Lines 47-57 explain that this is a disadvantage since it increases the processing/analysis time. To solve this problem Ishibashi teaches arranging the analysis modules in a parallel or serial manner and transferring the sample cups to the module that performs the required analysis/analyses without respect to the order in which the sample cups were supplied with sample (see column 2, lines 11-57). In other words the samples are sent directly to the analysis modules that are required by providing a bypass path around analysis modules that are unnecessary. Lines 58-60 teach that this allows the apparatus to operate all of the analyzing modules efficiently without waste of time.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to incorporate the teaching of Ishibashi into the Hutchins apparatus because of the ability to operate each analysis/processing module efficiently and reduce wasted time due to the successive treatment of the samples as taught by Ishibashi.

6. Claims 1-74 are rejected under 35 U.S.C. 103(a) as being unpatentable over Amano (US 4,835,707 in view of Kedar (US 6,323,035), Ishibashi (US 5,087,423 as explained above) and Stylli (US 5,985,214). In the patent Amano teaches an automatic analysis method of and apparatus for the full automation of an enzyme reaction analysis from the pretreatment step of

the reaction to the data processing step, wherein the operation of the pretreatment step is arranged to be sequentially performed on many samples with full automation by the use of robots (the robot shown is a rotational robot, 20) and computers to improve savings efficiency and measurement accuracy. Also, the pretreatment steps of weighing samples in many sample tubes, adding the given amount of solvent corresponding to the weighing value and placing the samples into the dissolution vessel to dissolve the sample in the solvent are adapted to be sequentially performed with full automation with the use of the robot, computer and electronic balance. Furthermore, the filtration, concentration and the injecting operations into the HPLC are automatically performed. The automatic apparatuses are coupled to each other so that the filtration, concentration, injecting operations are allowed to be sequentially performed with full automation using an on-line system. The summary of the invention describes several stations for treating the samples and two separate rotation robots to move the samples and treat them. In particular the device includes a weighing and dissolution apparatus, grasping a sample tube retained in a rack with a chuck provided on a movable arm of a first automatic robot for weighing the sample with an electronic balance, adding a predetermined amount of solvent to the sample in accordance with the weighing value of the sample, placing the sample tube into the dissolution vessel to dissolve the sample after the addition of solvent, moving the sample tube containing the dissolved sample onto a rack for dilution provided on a dilution and reacting apparatus; with the dilution and reacting apparatus, grasping a nozzle of a dilution dispenser, a sampling pipetter or an enzyme reaction mixture dispenser with the chuck of a second automatic robot to move the nozzle into the sample tube retained on the dilution rack or the reaction tube retained on a rack in an incubator, adding the diluted solution from the dilution dispenser into the sample tube located in the dilution rack to perform the diluting operation by a given amount, taking a sampling of the diluted solution from the sample tube with the sampling pipetter to inject it into the reaction tube, sequentially injecting enzymes and factors necessary for the enzyme reaction into the reaction tube at intervals of a given time, grasping the reaction tube with the second robot to move it into the preservation vessel after the reaction; grasping the reaction tube retained in the preservation vessel with the second robot to place it in the position of a reaction mixture sampling needle disposed in a filtration, concentration and analysis apparatus, filtering the reaction mixture through a filtration unit after the sampling operation of

reaction mixture with the sampling needle, feeding eluate into a concentration column after adsorption of the filtrate onto the concentration column, automatically injecting it into an analysis column for analysis by a HPLC, processing the obtained data by a data processing apparatus; and automatically controlling the operations of the first and second robots in accordance with a program input into a computer to automatically perform all of the operations from weighing to analysis. Amano does not teach a plurality of modules, multi-well plates as sample holders or non-sequential treatment of the samples

In the patent Kedar teaches systems and methods for handling multi-well plates. In one example a system is provided with a rotational robot having a base member and at least one arm. The arm includes a grasping mechanism which is adapted to grasp the plate. Further, the grasping mechanism is configured to receive the plate in a repeatable and known location such that the location of each well relative to the grasping mechanism is known by the robot. The invention relates generally to the field of device handling and manipulation, and particularly to the handling and manipulation of multi-well plates. In one particular aspect, the invention provides for the transport of multi-well plates to precise and known locations at various processing or evaluation stations. The use of multi-well plates to facilitate the performance of various chemical and biological procedures has become widely accepted. Such multi-well plates are typically rectangular in geometry and have a two dimensional array of wells (8 by 12 or 96 wells). To accommodate the performance of various procedures, the wells of such plates are configured to receive various chemicals or substances. One common procedure is the performance of assays where various chemicals or substances are introduced into the wells and any reactions are evaluated. One type of assay evaluation may proceed by placing the plate above a camera to detect an emitted signal from the wells. When using multi-well plates, it is often desirable to efficiently deliver and/or remove various chemicals or substances into or from the wells. This often requires the plate to be moved to various pieces of processing equipment for filling or removal. Further, the plates may also need to be transported to evaluation equipment for detection or other evaluation. When introducing or removing fluids or substances into or from the wells, and when evaluating the substances within the wells, the wells typically need to be aligned with distal tips, detection devices and the like. However, since various pieces of equipment may be needed to complete a procedure, each time the plate is moved to a different

piece of equipment, the plate will need to be properly oriented according to the specifications of the given piece of equipment. For example, many types of fluid delivery equipment include a stage on which the plate is placed. Often a robot is employed to grasp the plate and move the plate to the stage. However, such robots typically have a pair of grasping fingers that grasp the plate in an arbitrary manner and then place the plate on the stage. Once on the stage and removed from the robot, the dispensing tips will need to be aligned with the wells in the plate. Such a system is often burdensome and time consuming. Moreover, as it becomes more desirable to increase the numbers of wells in the plate while reducing their size, it becomes more difficult to precisely align the wells with various pieces of equipment. For example, many types of filling equipment are provided with 96 dispensing tips. If an 864 well plate is placed on a stage which can move only in the vertical direction, it is difficult, if not impossible, for the 96 dispensing tips to fill all of the 864 wells while the plate remains fixed on the stage. Hence, it would be desirable to provide systems, devices and methods to facilitate the transport of multi-well plates between various pieces of equipment in a manner such that the wells may be efficiently accessed or evaluated. The Kedar apparatus is taught as fulfilling this desire.

In the patent Stylli teaches systems and methods for rapidly identifying useful chemicals in liquid systems and uses automated and integratable workstations for identifying chemicals having useful activity. The present invention is also directed to chemical entities and information (e.g., chemical or biological activities of chemicals) generated or discovered by operation of workstations of the present invention. The present invention includes automated workstations that are programmably controlled to minimize processing times at each workstation and that can be integrated to minimize the processing time of the liquid samples from the start to finish of the process. Systems and methods for rapidly identifying chemicals with biological activity in samples, especially small liquid samples, can benefit a number of different fields. For instance, the agrochemical, pharmaceutical, and cosmetic fields all have applications where large numbers of liquid samples containing chemicals are processed. Currently, many such fields use various strategies to reduce processing times, such as simplified chemistry, semi-automation and robotics. While such strategies may improve the processing time for a particular type of liquid sample, process step or chemical reaction, such methods or apparatuses can seldom integrate the entire process, especially the generation or detection of chemical events in small volumes. Such

apparatus are also often limited in their application, since many of them are designed for, and dedicated to, a particular type of liquid sample or chemical reaction. In most processes involving liquid samples, as the complexity of the liquid sample processing increases the process time per sample increases. Although, some very simple chemical reactions or liquid processing methods can achieve extremely high throughput rates, such as in the manufacturing of containerized liquids, complicated processing of liquids is typically several orders of magnitude slower. In some instances, the processing of liquid samples, such as in pharmaceutical arts, which usually demands complicated liquid processing for drug discovery, can obtain throughput rates of approximately 3,000 samples per day. This type of processing in general, however, uses liquid sample volumes on the order of 100 to 200 microliters, which often requires relatively large amounts of exotic and expensive reagents, and does not typically incorporate automated access to large stores of liquid reagents. Consequently, there is a need to provide components, systems and methods for rapidly processing liquid samples at high throughput rates, particularly liquid samples of microliter volumes, one to ten microliters, to identify chemicals with useful activity. Columns 2-3 teach several modules for the Stylli apparatus. Columns 3-5 provide several definitions of which adaptive routing, daughter plate and parallel processing are relevant to the ability to increase the through put of the device. Column 18, lines 33-50 teach various rates of throughput going up to 10 million wells processed in a day. The following paragraph explains how parallel processing can be used to increase the throughput.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to provide several modules as taught by Stylli or Ishibashi and incorporate parallel processing of Stylli or the non sequential sample transport of Ishibashi into the Amano apparatus because of the ability increase the throughput as taught by Stylli and to operate each analysis/processing module efficiently and reduce wasted time due to the successive treatment of the samples as taught by Ishibashi. It would have been obvious to one of ordinary skill in the art at the time the invention was made to utilize the multi-well plates of Stylli or Kedar along with the plate grasping mechanism of Kedar into the Amano device because of the ability to increase throughput or facilitate the efficient processing of samples as taught by Kedar and Stylli.

7. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. The additionally cited art teach automated analysis apparatus with rotational robots.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arlen Soderquist whose current telephone number is (571) 272-1265 as a result of the examiner moving to the new USPTO location. The examiner's schedule is variable between the hours of about 5:30 AM to about 5:00 PM on Monday through Thursday and alternate Fridays.

A general phone number for the organization to which this application is assigned is (571) 272-1700. The fax phone number to file official papers for this application or proceeding is (703) 872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Arlen Soderquist
September 14, 2004

ARLEN SODERQUIST
PRIMARY EXAMINER